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Load/strain distribution between ulna and radius in the mouse forearm compression loading model

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ABSTRACT

Finite element analysis (FEA) of the mouse forearm compression loading model is used to relate strain distributions with downstream changes in bone formation and responses of bone cells. The objective of this study was to develop two FEA models – the first one with the traditional ulna only and the second one in which both the ulna and radius are included, in order to examine the effect of the inclusion of the radius on the strain distributions in the ulna. The entire mouse forearm was scanned using microCT and images were converted into FEA tetrahedral meshes using a suite of software programs. The performance of both linear and quadratic tetrahedral elements and coarse and fine meshes were studied. A load of 2 N was applied to the ulna/radius model and a 1.3 N load (based on previous investigations of load sharing between the ulna and radius in rats) was applied to the ulna only model for subsequent simulations. The results showed differences in the cross sectional strain distributions and magnitude within the ulna for the combined ulna/radius model versus the ulna only model. The maximal strain in the combined model occurred about 4 mm toward the distal end from the ulna mid-shaft in both models. Results from the FEA model simulations were also compared to experimentally determined strain values. We conclude that inclusion of the radius in FE models to predict strains during *in vivo* forearm loading increases the magnitude of the estimated ulna strains compared to those predicted from a model of the ulna alone but the distribution was similar. This has important ramifications for future studies to understand strain thresholds needed to activate bone cell responses to mechanical loading.

1. Introduction

The *in vivo* forearm compressive loading model is widely used to study bone formation in response to mechanical loading [1–10]. *In vivo* mouse forearm compression loading experiments are typically conducted by applying a cyclic load that produces a particular maximum bone surface strain in the ulna. The desired surface strain is achieved by calibrating load levels using a strain gage attached to the ulna surface and then applying different magnitudes of loads to determine the resultant strain and displacement values. In order to understand the mechanisms by which *in vivo* forearm loading may be triggering an osteogenic response, finite element analysis (FEA) models have been constructed to assess general strain distributions within the bone tissue that result from the applied external mechanical loading. FEA models of the mouse tibia [11,12], rat ulna [13–15] and turkey ulna [16] have all been described by various researchers. However, the mouse ulna models generally do not include the radius, and consequently use estimates of load sharing between the ulna and radius for model boundary conditions to predict strain distributions within the ulna. These estimated strain distributions are commonly used to assess the relationship between mechanical stimulation and the osteogenic response in bone. Silva et al. [12] used a tibia-fibula FEA model for simulating their three point bending experiments.

Osteocytes located within the bone matrix appear to respond to load in a heterogeneous manner. It was originally hypothesized [17] that Lrp5 and the Wnt/β-catenin signaling pathway were involved in bone responsiveness to mechanical loading. This has been confirmed in a number of studies from our lab and other investigators [18–21]. Recent findings in our laboratory have shown that activation of β-catenin signaling in bone in response to mouse forearm compression mechanical loading occurs first in osteocytes and then propagates to surrounding osteocytes and eventually to cells on the bone surfaces where new bone formation will occur [22]. However, within a given uniform strain field as predicted by finite element analysis (FEA), not all osteocytes activate β-catenin signaling, even ones that are adjacent to each other [22] demonstrating a heterogeneous response. Nicolella et al. [23] have previously shown that

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the strain fields in bone slices around osteocytes can vary dramatically within a relatively small spatial region. This heterogeneity in the osteocyte response suggested to us that the current FEA models of the ulna do not adequately capture the strain fields at this microscale level. In order to eventually achieve that goal, the purpose of this study was to lay down a foundation by constructing a first generation FEA model of the mouse forearm that included both the ulna and radius, called the ulna radius model (URM), and compare load sharing, strain magnitudes and distributions with a corresponding ulna only model (UM).

2. Methods

2.1. Finite element modeling

Finite element models of a TOPGAL mouse forearm were developed from microCT images with a 65 μm resolution in plane and the axial slices were 12 μm apart (Scanco MicroCT, Scanco Medical, Basserdorf, Switzerland). The TOPGAL mouse was used so that future studies can be performed comparing the osteocyte biological response with magnitude of strain at the cellular level. This mouse is normal except for expression of a reporter for activation of the β-catenin pathway [24]. The microCT (μCT) scan images (1100 slices) were imported into Slicer3D v3.2.1 (www.slicer.org) [25,26] where both the endosteal and periosteal cortical boundary of each bone were manually traced. The resulting segmented images were imported into GeoMagic Studio 9 (www.geomagic.com) where the 3D object underwent smoothing, patching, curve-fitting, and surface mapping before the final CAD model was created.

Meshing was performed using an automatic mesh generation process using ABAQUS v6.10-1 CAE using tetrahedron elements. Both four node and ten node tetrahedron elements were each used to generate two different mesh densities (coarse mesh and fine mesh) that were subsequently used to investigate finite element solution convergence (mesh convergence). The ulna plus radius coarse mesh was constructed using ten node tetrahedral elements and had 19,550 nodes and 11,405 elements. Its counterpart, the fine mesh with ten node tetrahedral elements had 192,674 nodes and 124,145 elements. On the other hand, the coarse four node tetrahedral mesh had 6048 nodes and 23,818 elements and the fine mesh with four node tetrahedral elements had 27,468 nodes and 124,145 elements.

Before the static analysis was conducted, a coordinate transformation was applied to the model such that the ulna was aligned in the vertical direction (z-axis) in order to be consistent with the alignment of the ulna during *in vivo* loading experiments. The model loading boundary conditions consisted of a concentrated load of 2 N along the z-axis applied at the proximal end of ulna. A fixed boundary condition was imposed on selected nodes at the distal end of both the ulna and radius. Linear one dimensional spring elements were used to simulate the ligament that connects the ulna and radius at both the ends of the radius. A spring constant of 1400 N/mm was used [27]. While we did not explicitly determine the spring constant for this study, Silva et al. [12] compared models with rigid fusion and no constraint between the tibiofibular joint and found that the difference in strain values at the mid-diaphysis region was only three percent.

2.2. Material properties of bone

A wide range of values for the mechanical properties, especially the elastic modulus and density, of rat and mouse bones have been reported [28–35] in literature. For instance, the elastic modulus of the femur was experimentally determined to range from 8 GPa to 34 GPa by bending tests [14,36] or through nano-indentation technique [30,34,37–39].

Although no experimentally obtained data for the biomechanical properties of the mouse ulna/radius used in this study were available, we assigned an elastic modulus of 20 GPa to ulna and 18 GPa to radius in our FE analysis based on the values reported in the literature [12]. The cortical bone mineral density determined by μCT of the mouse forearm used to generate the models was 1168 kg/m^3 for the ulna and 1172 kg/m^3 for the radius, and Poisson's ratio was set at 0.30 and 0.33 for ulna and radius, respectively.

The final finite element models were imported into two commercially available FEA programs (ABAQUS v 6.10-1 [Simulia, Providence, RI], and LS-DYNA v971 [LSTC Inc., Livermore, CA]) to conduct the FE analyses/simulations. For LS-DYNA element formulation number 10 (4-noded tetrahedron with 1 integration point) was used for the four node tetrahedral and element formulation 16 (10-noded tetrahedron with 4 or 5 integration points) was used for the 10 node tetrahedral mesh. The exact same load and boundary conditions were applied for each analysis performed with each program.

2.3. Ex vivo strain gaging

Forearm experimental data using TOPGAL mice were obtained from ex vivo loading using the Bose ElectroForce 3220 system. Maximum compressive strains were measured using a strain gage (Vishay EA-06-015DJ-120/LE) applied to the ulna (at 2 mm distal to the ulna mid-shaft on the medial surface and at a site 5 mm distal to the end of the olecranon process on the lateral surface). The forearms were kept hydrated with phosphate buffered saline throughout the measurements. After application of strain gage, loading was conducted on the right forearm at 2 Hz, using a haversine waveform for 15 cycles. Loading is conducted at 0.7, 1.2, 1.7, 2.2, 2.7 and 3.1 N for the intact forearm. Strains in the last five cycles were averaged.

3. Results

3.1. Model validation

Fig. 1 shows the displacement contours calculated using ABAQUS and LS-DYNA. The contour profiles determined by both methods demonstrate a high degree of similarity. Maximum displacements predicted by each model are compared directly in Table 1 for the two FEA codes using each type of mesh. Overall, there was very good agreement between these programs. Using ABAQUS, the difference between the coarse mesh maximum displacement (0.167 mm for the 10 noded tetrahedron) and the corresponding fine mesh value (0.183 mm) was 11.36% despite increasing the number of elements 10.89 fold. Models constructed using the quadratic 10-node tetrahedron element (ABAQUS and LS-DYNA) predicted larger deformation (0.1833 and 0.1810 mm, respectively) compared to their 4-node counterpart (0.1183 and 0.1436 mm, respectively). In order to check the sensitivity of the displacement values to the differences in the elastic modulus of the ulna and radius (20 GPa and 18 GPa) and Poisson's ratio (0.3 and 0.33) several combinations were run and the difference in displacement values was less than 1%.

However, the principal stress and strain values showed a higher percentage of difference between the fine and coarse mesh models. At an almost identical location the maximum axial stress values were 71 MPa and 52.8 MPa in compression for the fine and coarse meshes respectively and the axial strain values were 3510 and 2613 microstrain respectively. The stress and strain values are slower to converge compared to displacements. A difference of about 25%